

Current therapies for MS

ABC Treatments				
Condition/Symptom	Generic Name	Comments	Brand Name	Manufacturer
Relapsing-Remitting MS, Secondary Progressive MS with relapses	Interferon Beta 1a	30 mcg intramuscular once per week self-injection	Avonex	Biogen
		44 mcg subcutaneous 3 times per week self-injection	Rebif	Ares-Serono
	Interferon Beta 1b	Subcutaneous self-injection once every two days	Betaseron Betaferon	Berlex Schering
Relapsing-Remitting MS	Glatiramer Acetate	20mg subcutaneous daily self-injection	Copaxone	Teva-Marion
Chemotherapeutic Agents				
Condition/Symptom	Generic Name	Comments	Brand Name	Manufacturer
Secondary Progressive MS, Worsening Relapsing-Remitting MS	Mitoxantrone	Intravenous every 3 months for about 2 to 3 years	Novantrone	Immunex
Potential, unlicensed treatments for Secondary Progressive MS and Worsening Relapsing-Remitting MS	Azathioprine	Anti-cancer treatments - currently unlicensed for use with MS	Imuran	Glaxo-Smith-Kline
	Cyclophosphamide	Anti-cancer treatments - currently unlicensed for use with MS	Cytosan, Neosar	Bristol-Myers Squibb
	Cyclosporine	Anti-cancer treatments - currently unlicensed for use with MS	Sandimmune	Novartis Pharma

Methotrexate	Anti-cancer treatments - currently unlicensed for use with MS	generic	<u>Mylan</u>
Cladribine	Anti-cancer treatments - currently unlicensed for use with MS	Leustatin	

Corticosteroids & ACTH

Condition/Symptom	Generic Name	Comments	Brand Name	Manufacturer
Acute relapses in Relapsing-Remitting MS and occasionally Secondary Progressive MS	MethylPrednisolone	Intravenous high doses tapered off	Depo-Medrol Solu-Medrol	<u>Pharmacia</u>
	Prednisone	Oral administration	Deltasone	<u>Pharmacia</u>
	Prednisolone	Intravenous administration	Delta-Cortef	<u>Pharmacia</u>
	Dexamethasone	Oral administration	Medrol Decadron	<u>Pharmacia</u> <u>Merck</u>
	Adreno-corticotrophic Hormone (ACTH), Corticotropin	Use largely replaced by synthetic corticosteroids	Acthar	<u>Roche</u> , Rhone-Poulenc Rorer

Pain/Altered Sensation (Dysaesthesia)

Condition/Symptom	Generic Name	Comments	Brand Name	Manufacturer
Neuropathic/neurogenic pain (pain that arises from nerve dysfunction and not as a result of injury e.g. Trigeminal Neuralgia)	<u>Carbamazepine</u>	Anti-convulsant	Tegretol, Epitol, Atretol, Carbatrol	<u>Ciba</u>
	Gabapentin	Anti-convulsant	Neurontin	<u>Pfizer</u>
	Topiramate	Anti-convulsant	Topamax	<u>Ortho-McNeil</u>
	Zonisamide	Anti-convulsant	Zonegran	<u>Elan</u>
	Phenytoin		Dilantin	
	Desipramine		Norpramin	
	Amitriptyline	Tricyclic antidepressant	<u>Elavil</u>	<u>AstraZeneca</u>
	Imipramine	Tricyclic	Tofranil,	<u>Ciba Geigy</u>

		antidepressant	Imavate, Janimine	
	Doxepin	Tricyclic antidepressant	Sinequan, Adapin, Triadapin, Zonalon	
	Protriptyline	Tricyclic antidepressant	Vivactil	
	Cannabis and synthetic cannabinoids	Illegal in many parts of the world	Marinol	
Pain associated with poor circulation	Pentoxifylline		Trental	
'flu-like symptoms associated with Beta Interferon injections	Ibuprofen		Neurofen <i>US versions</i>	
	Aspirin		generic	
	Acetaminophen	Often formulated with alkaloid pain killers like codeine and hydrocodone	generic	
Paroxysmal itching	Hydroxyzine		Atarax	

Compounds for MS in Phase II and III

Phase III

- Alemtuzumab (brand name: Campath; under development by Genzyme and Bayer Schering) is a monoclonal antibody currently already used in the treatment of chronic lymphocytic leukemia and T-cell lymphoma.
- BG00012 (an oral fumarate ester under development by Biogen; anticipated brand name Panaclear).
- Cladribine (under development by Merck Serono; anticipated brand name: Movectro) is an antineoplastic compound with immunosuppressive effects. It is already currently used as an intravenous infusion to treat hairy cell leukemia (leukemic reticuloendotheliosis).
- Dirucotide (MBP8298), a synthetic myelin basic protein (MBP) consisting of 17 aminoacids, is currently in FDA fast-track for approval for SPMS.

- Fingolimod (under development by Novartis) is a sphingosine-1-phosphate receptor modulator for oral use.
- Laquinimod (under development by Teva and Active Biotech) is an immunomodulatory substance developed as an orally available disease modifying treatment in multiple sclerosis.
- Rituximab, trade names Rituxan and MabThera, is an anti-CD20 monoclonal antibody previously used against cancer, has shown damaging lesions reduction by 91% and relapses by 58%.
- Teriflunomide, the active metabolite of the antirheumatic drug leflunomide, is currently under investigation for treatment of MS.

Phase II

- ATL1102 (under development by Teva and Antisense Therapeutics) is a second-generation antisense inhibitor of CD49d, a subunit of VLA-4
- CDP323 (under development by UCB S.A. and Biogen) is a compound for oral intake acting against $\alpha 4$ -integrin, i.e., it has the same mechanism of action as natalizumab.
- Daclizumab (brand name Zenapax; under development by Biogen and PDL) is an anti-IL2 monoclonal antibody and an immunosuppressant used to prevent rejection after organ transplantation..
- Estradiol and estrogen receptors(ER):
- Inosine: Inosine is a compound that has shown interesting preliminary results in phases I and II clinical trials. Two different mechanisms of action have been proposed. First, it produces uric acid after ingestion, which is a natural antioxidant; second, it has been shown to induce axonal rewiring in laboratory animals with stroke, and spinal cord injury[. However it can cause health problems in a long-term treatment mainly kidney stones.
- Tovaxin. Also a vaccine against T-Cells, which in this case consist of attenuated autoreactive T cells. It is developed by Opexa Therapeutics, (previously known as PharmaFrontiers
- Ocrelizumab, Anti-CD20 humanized monoclonal antibody, whose mechanism of action targets B-Cells, like Rituximab.
- Ofatumumab, other anti-CD20 monoclonal antibody, .
- Stem cell transplantation was found feasible in a phase I/II study in 21 patients with relapsing-remitting MS not responsive to interferon beta. It involves collecting some of the patient's own peripheral blood stem cells, giving low-intensity chemotherapy to eliminate auto-reactive lymphocytes, and then reinfusing the stem cells.
- BAF312, NOVARTIS' BAF312 is a sphingosine-1-phosphate receptor modulator for oral use that is currently (June 08, 2009) in Phase II trial.